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Original Article

Sleep duration and cardiometabolic risk factors among individuals with type 2 diabetes

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ABSTRACT

Objective: To examine the association between sleep duration and cardiometabolic risk factors among individuals with recently diagnosed type 2 diabetes ($n = 391$).
Methods: Sleep duration was derived using a combination of questionnaire and objective heart rate and movement sensing in the UK *ADDITION-Plus* study (2002–2007). Adjusted means were estimated for individual cardiometabolic risk factors and clustered cardiometabolic risk (CCMR) by five categories of sleep duration.
Results: We observed a J-shaped association between sleep duration and CCMR – individuals sleeping 7 to <8 h had a significantly better CCMR profile than those sleeping ≥9 h. Independent of physical activity and sedentary time, individuals sleeping 7 to <8 h had lower triacylglycerol (0.62 mmol/l (0.29, 1.06)) and higher high-density lipoprotein (HDL)-cholesterol levels (0.23 mmol/l (0.16, 0.30)) compared with those sleeping ≥9 h, and a lower waist circumference (7.87 cm (6.06, 9.68)) and body mass index (BMI) (3.47 kg/m^2 (2.69, 4.25)) than those sleeping <6 h. Although sleeping 7 to <8 h was associated with lower levels of systolic and diastolic blood pressure, HbA_{1c}, total cholesterol, and low-density lipoprotein (LDL)-cholesterol, these associations were not statistically significant.
Conclusions: Sleep duration has a J-shaped association with CCMR in individuals with diabetes, independent of potential confounding. Health promotion interventions might highlight the importance of adequate sleep in this high-risk population.

1. Introduction

It is currently recommended that adults should aim to get 7–9 h of sleep each day [1]. However, a large majority of adults report sleeping less than this, a trend which has become increasingly prevalent in modern society. Recent data from 'The Great British Bedtime Report' revealed that in 2013, 70% of the adult population slept for ≤7 h, and 33% slept for <6 h per night compared to 27% in 2010 [2]. Sleep duration in adult Americans follows a similar declining trend [3]. In the last decade, an increasing number of laboratory and epidemiological studies have linked short sleep duration with increases in hunger and appetite [4], decreased glucose tolerance [5] and increased risk of weight gain [6,7], obesity [6,7], hypertension [8,9], type 2 diabetes [10], and cardiovascular outcomes [11].

While laboratory studies provide important insights into the potential pathways linking acute short sleep duration with cardiovascular health, the major limitations are that they are conducted in artificial settings and usually have small sample sizes [12]. Whether prolonged short sleep duration is associated with factors predisposing to cardiovascular disease in free-living populations remains unclear. Although a number of epidemiological studies have examined associations between habitual sleep duration and cardiovascular health outcomes, they have traditionally used self-report measures of sleep duration [13] which are prone to error and bias and which only have moderate agreement with objectively assessed sleep duration [14]. Furthermore, though physical activity and sedentary time may confound the association between sleep duration and cardiovascular health [15,16], only a small number of studies have adjusted for self-reported physical activity [17,18]; to our knowledge, no studies have adjusted for objective measures of physical activity and sedentary time. These important limitations preclude a clear understanding of the potential role that sleep duration may have in cardiovascular health. Finally, few studies have

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examined the role of sleep duration among individuals with type 2 diabetes, who are, as a consequence, at a higher risk of developing cardiovascular diseases [17–21]. An improved understanding of this relationship will inform future intervention programmes aimed at identifying and managing high-risk individuals.

The objective of the current study was to quantify the association between sleep duration and cardiometabolic risk factors derived using a combination of self-report questionnaire and objectively measured free-living data, independent of potential confounding by physical activity and sedentary time, among a population at high risk of developing cardiovascular disease.

2. Methods

The design and rationale for the *ADDITION-Plus* study have been reported previously (2002–2007) [22]. In brief, *ADDITION-Plus* is a randomised controlled trial nested within the intensive treatment arm of the *ADDITION-Cambridge* study, which evaluated the efficacy of a facilitator-led, theory-based behaviour change intervention for recently diagnosed type 2 diabetes patients. Thirty-four general practices (GPs) in East Anglia participated. Eligible individuals included those aged 40–69 years diagnosed with diabetes following screening in the *ADDITION* study or clinically diagnosed in the last three years in participating GP surgeries. Exclusion criteria included women who were pregnant or lactating or anybody with a psychotic illness or an illness with a likely prognosis of <1 year. Out of 1109 eligible individuals, 478 agreed to participate in *ADDITION-Plus* and were individually randomised to receive either intensive treatment alone ($n = 239$) or intensive treatment plus a facilitator-led individual behaviour change intervention ($n = 239$). All participants gave written informed consent, and the study was approved by the Eastern Multi-Centre Research Ethics Committee (reference number: 02/5/54). The trial is registered as ISRCTN 99175498.

2.1. Assessment of physical activity and sleep duration

Participants' activity intensity was assessed using a combined heart rate and movement sensor (Actiheart, Cam Ntech, Cambridge, UK) worn continuously for four days at 30-s resolution, as described in detail elsewhere [23]. A graded treadmill walk test was used to individually calibrate heart rate, as described elsewhere [15,24]. For participants who did not complete an individual calibration test, all valid calibration tests in the rest of the sample were used to derive an age, sex, beta blocker, and sleeping heart-rate-adjusted group calibration equation for the translation of heart rate to activity intensity. Heart rate data collected during the free-living period were processed using noise classification followed by Gaussian robust regression [25] and the average activity intensity (J min^{-1} kg^{-1}) was estimated using a branched equation framework [26]. Resulting time-series data were summarised into physical activity energy expenditure (PAEE; kJ kg^{-1} day^{-1}) and sedentary time whilst minimising diurnal information bias caused by non-wear periods (segments of non-physiological data). Sedentary time was defined as a metabolic equivalent of task (MET) value of <1.5 in accordance with the current convention [27] using the Oxford estimate of resting metabolic rate (RMR) to define 1 MET [28]. To derive sleep duration, time-series data from the combined heart rate and movement sensor were summarised after constraining assessment within each participant's mean self-reported wake time and bedtime (self-reported using open-ended questions asking 'at what time do you normally get up?' and 'at what time do you normally go to bed?' on weekdays and on weekend days [29]) in combination with the requirement that intensity was ≤1.04 METs. This intensity threshold was applied according to recent research demonstrating that values below this MET cut-point are symptomatic of being in a reclined posture (indicative of sleep) as opposed to a seated posture [30]. The appropriateness of this method was verified by a visual inspection by overlaying self-reported wake time and bedtime on the objective time-series data.

2.2. Outcome measurements

Body weight and height were measured in light clothing and without shoes using a scale (SECA, UK) and a fixed rigid stadiometer, respectively. The body mass index (BMI) was calculated as weight in kilograms divided by height in metres squared (kg/m^2). Waist circumference was calculated as the average of two measurements taken halfway between the lowest point of the rib cage and the anterior superior iliac crests while standing. Blood pressure was calculated as the mean of three measurements performed after 10 min of rest and with participants seated with a cuff placed on the predominant arm at the level of the heart, using an automatic sphygmomanometer (Omron M4, UK). HbA_{1c} was measured in venous samples using an ion-exchange high-performance liquid chromatography method (Tosoh Bioscience, Redditch, UK). Serum triacylglycerol, total cholesterol, high-density lipoprotein (HDL)- and low-density lipoprotein (LDL)-cholesterol were measured using enzymatic techniques (Dade Behring Dimension analyser, Newark, DE, USA). All measures were carried out by trained staff following standard operating procedures and who were unaware of participants' sleep patterns.

A summary clustered cardiometabolic risk score (CCMR-score) was created, incorporating measures of central obesity (waist circumference), dyslipidaemia (fasting triacylglycerol and HDL-cholesterol), hypertension (systolic blood pressure) and hyperglycaemia (HbA_{1c}). Individual measures were standardised (i.e., *z*-scores were computed: $z = (\text{value} - \text{mean})/\text{standard deviation (SD)}$) after log transformation (ln) of triacylglycerol due to a non-normal distribution. Next, individual *z*-scores were summed after inverting HDL-cholesterol values. CCMR was also calculated without the inclusion of BMI ($CCMR_{noBMI}$), thereby allowing the examination of the association of sleep duration on CCMR independent of BMI.

2.3. Covariates

PAEE and sedentary time were assessed using combined heart rate and movement sensing (see: *Assessment of physical activity and sleep duration*). Standardised self-report questionnaires were used to collect information on socio-demographic characteristics, smoking status and prescribed medication. Total energy and alcohol intake were assessed using a validated food frequency questionnaire [31]. As psychological disorders can contribute to chronic sleep deprivation, and are positively associated with weight gain [32], we adjusted for the mental components of health status using the short-form-36 (SF-36) health survey questionnaire [33].

Complete data on objectively measured sleep duration, PAEE, time spent sedentary, metabolic risk factors, and potential confounding variables were available for 391 participants.

2.4. Statistical analysis

The data for this analysis were treated as a cohort and not analysed by trial arm because the intervention used in *ADDITION-Plus* was not designed to influence sleep duration and no evidence of interaction by trial arm was found in the proceeding multivariate analyses (all *p* interaction ≥0.09). Descriptive characteristics of the participants were summarised by categories of sleep duration (<6 h, 6 to <7 h, 7 to <8 h, 8 to <9 h and ≥9 h) using means with SDs, medians with interquartile ranges or frequencies. *P* for trend, Kruskal–Wallis, and chi-squared tests were used to examine

differences in participant characteristics across categories of sleep duration.

We examined associations between sleep duration categories (<6 h, 6 to <7 h, 7 to <8 h, 8 to <9 h and ≥9 h) and CCMR, CCMR $_{noBMI}$, waist circumference, BMI, systolic and diastolic blood pressure, HbA_{1c}, triacylglycerol, total cholesterol, and HDL- and LDL-cholesterol using multivariate linear regression analyses. Triacylglycerol values were log-transformed (ln) for statistical analysis due to a non-normal distribution. We estimated the adjusted means and 95% confidence intervals (CIs) of CCMR, CCMR $_{noBMI}$, waist circumference, BMI, systolic and diastolic blood pressure, HbA_{1c}, triacylglycerol (ln), total cholesterol, and HDL- and LDL-cholesterol for each sleep category and tested for linear and nonlinear trends across categories using the post-estimation polynomial 'contrast' command in Stata. We included potential confounders in the models based on previously published associations, biological reasoning and statistical associations between exposure and outcomes in the current dataset. All regression models are presented adjusted for age, sex and trial arm (age–sex adjusted) and adjusted for age, sex, trial arm, occupational socio-economic class, PAEE, time spent sedentary, smoking status, alcohol intake, daytime tiredness, mental health score, and sleep affecting medication, for example, beta blockers, sleeping tablets and minor tranquilisers [34] (multivariate adjusted). Triacylglycerol values were back-transformed and reported as adjusted geometric means and their 95% CIs. When the outcome of interest was blood pressure, HbA_{1c}, triacylglycerol or HDL- and LDL-cholesterol, we additionally adjusted for use of anti-hypertensive, glucose-lowering or lipid-lowering medication, respectively. For CCMR, we adjusted for use of anti-hypertensive, glucose-lowering and lipid-lowering medications, and additionally for BMI when examining CCMR $_{noBMI}$. The variance inflation factor did not exceed 4 in any of the models, indicating the absence of multicollinearity. To investigate differences between sleep duration categories, we used Dunnett's significant difference post hoc test to compare each category of sleep duration with those sleeping 7 to <8 h/night (comparison category). A duration of 7 to <8 h/night of sleep was chosen as the comparison category a posteriori based on this category having the lowest CCMR risk profile. We formally examined whether associations between sleep duration categories and CVD risk factors were modified by sex by entering cross-product terms in the multivariate models.

In sensitivity analyses, we assessed whether our findings were sensitive to: (1) the inclusion of energy intake in all multivariate models, (2) inclusion of waist circumference as opposed to BMI in all multivariate models adjusted for BMI and (3) using a cut-point of ≤1.04 METs for the definition of sleep as opposed to a cut-point of ≤1.00 MET. All statistical analyses were performed using Stata/SE 13.1 (Stata-Corp, College Station, TX, USA).

3. Results

The mean (SD) age of study participants was 60.3 (7.4) years. Of the participants, 97.7% were of white European descent and 41.9% reported having a managerial job. More men than women ($n = 248$ vs. 143, respectively) met the inclusion criteria for the study and agreed to participate. The mean duration of diabetes did not differ across categories of sleep duration ($p = 0.43$). The percentage of study participants who slept <6 h and >9 h per night was 11.3% and 5.9%, respectively. Table 1 shows the characteristics of the study population by categories of sleep duration. Compared with participants with short sleep durations, participants with longer sleep durations were older, were more likely to be female and were less likely to be employed in a managerial position. When expressed in absolute terms, both PAEE and sedentary time decreased across increasing sleep categories. By contrast, when expressed relative to hours awake, participants sleeping 7 to <8 h/day had the highest PAEE level and spent the lowest proportion of the day sedentary. Sleep duration was weakly inversely correlated with sedentary time ($r = –0.22$; $p < 0.001$) and PAEE ($r = –0.26$; $p < 0.001$). Sedentary time was strongly inversely correlated with PAEE ($r = –0.73$; $p < 0.001$). The mean duration of valid combined heart rate and movement sensing data was 4.02 (SD: 0.40) days.

As shown in Table 2, after adjustment for age, sex and trial arm, participants sleeping 7 to <8 h/night had a lower CCMR and CCMR $_{noBMI}$ than all other sleep categories, which was significantly lower when compared with those sleeping ≥9 h/night ($p < 0.05$). The J-shaped associations between sleep duration and CCMR and CCMR $_{noBMI}$ remained after the additional adjustment for other potential confounding factors including objectively assessed physical activity, sedentary time, feelings of daytime tiredness, sleep affecting medication (p quadratic trend: 0.004) and BMI in the CCMR $_{noBMI}$ model (p quadratic trend: 0.025). After multivariate adjustment, sleep

Table 1
Characteristics of the UK *ADDITION-Plus* study (2002–2007) participants according to sleep duration.

	Sleep duration (h/day)					
	<6	6 to <7	7 to <8	8 to <9	≥9	*p* value
N	44	102	138	84	23	
Sleep duration (h/day)	5.2 (0.7)	6.6 (0.3)	7.4 (0.3)	8.4 (0.3)	9.5 (0.7)	
Age (years)	58.6 (6.5)	58.5 (7.4)	60.3 (7.2)	61.9 (7.5)	65.9 (5.4)	<0.001
Male (%)	77	75	66	48	26	<0.001
Duration of diabetes (years)	2.1 (2.3)	2.2 (1.7)	2.0 (1.8)	2.4 (2.1)	2.4 (2.2)	0.43
Sex-adjusted energy intake (kcal day^{-1})	1762 (492)	1834 (494)	1735 (490)	1651 (499)	1662 (499)	0.15
Total PAEE (kJ kg^{-1} day^{-1})	40.7 (17.7)	36.2 (17.4)	36.7 (16.2)	29.7 (16.0)	22.6 (8.2)	<0.001
PAEE/hour (kJ kg^{-1} woken hour^{-1})	2.17 (0.95)	2.07 (0.99)	2.22 (0.97)	1.91 (1.02)	1.55 (0.55)	0.005
Total sedentary time (h/day)	11.1 (2.8)	10.9 (2.6)	9.4 (2.5)	9.8 (2.0)	9.6 (1.8)	<0.001
Percentage woken hour^{-1} sedentary (%)	0.59 (0.15)	0.62 (0.15)	0.57 (0.15)	0.63 (0.13)	0.66 (0.12)	0.008
Managerial socio-economic class (%)	41	51	44	32	26	0.02
Current smoker (%)	20	19	10	10	17	0.15
Sex-adjusted alcohol intake (g/d)	11.2 (1.6)	6.5 (1.0)	6.6 (0.9)	9.6 (1.1)	7.8 (2.2)	0.03
Tiredness during the day (%)	34	32	23	27	17	0.33
Mental health score	73 (22)	78 (16)	79 (18)	75 (18)	80 (14)	0.27
Sleep medication user (%)	14	14	12	21	9	0.29
Use anti-hypertensive drugs (%)	70	76	67	73	87	0.28
Use hypoglycaemic drugs (%)	50	56	50	49	52	0.88
Use lipid-lowering drugs (%)	73	76	78	74	74	0.95

Values are expressed as means (SD) unless stated otherwise. *p* values are from *p* trend, Kruskal–Wallis and chi-squared tests, as appropriate.
Abbreviations: IQR = interquartile range. PAEE = physical activity energy expenditure.

Table 2
Adjusted means (95% CIs) for cardiovascular risk factors according to sleep duration categories for UK *ADDITION-Plus* study (2002–2007) participants.

	Sleep duration (h/day)					*p* for linear trend	*p* for quadratic trend
	<6	6 to <7	7 to <8	8 to <9	≥9		
N	44	102	138	84	23		
CCMR-score							
Age and sex adjusted	0.17 (–0.58, 0.92)	0.08 (–0.42, 0.58)	–0.44 (–0.86, –0.02)	–0.20 (–0.74, 0.35)	1.33 (0.27, 2.39)*	0.154	**0.005**
Multivariate adjusted	0.53 (–0.26, 1.32)	0.10 (–0.41, 0.61)	–0.39 (–0.81, 0.02)	–0.37 (–0.93, 0.18)	0.92 (–0.16, 2.00)	0.839	**0.004**
$CCMR_{noBMI}$							
Age and sex adjusted	–0.09 (–0.73, 0.55)	0.07 (–0.35, 0.49)	–0.34 (–0.69, 0.02)	–0.09 (–0.55, 0.37)	1.29 (0.39, 2.19)*	**0.032**	**0.011**
Multivariate adjusted	–0.05 (–0.74, 0.64)	–0.02 (–0.46, 0.43)	–0.29 (–0.65, 0.07)	–0.07 (–0.55, 0.42)	1.22 (0.28, 2.17)*	0.075	**0.013**
Multivariate + BMI	–0.24 (–0.94, 0.46)	–0.06 (–0.50, 0.38)	–0.27 (–0.63, 0.09)	0.02 (–0.46, 0.51)	1.31 (0.37, 2.25)*	**0.024**	**0.025**
Waist (cm)							
Age- and sex-adjusted	112.92 (109.11, 116.72)	109.95 (107.42, 112.48)	108.03 (105.90, 110.16)	107.41 (104.62, 110.19)	108.50 (103.08, 113.92)	0.118	0.193
Multivariate adjusted	116.18 (112.38, 119.98)*	111.08 (108.64, 113.53)	108.31 (106.32, 110.30)	104.98 (102.28, 107.67)	104.42 (99.19, 109.64)	**<0.001**	0.201
BMI (kg/m^2)							
Age- and sex-adjusted	33.60 (31.97, 35.23)	32.42 (31.34, 33.51)	31.74 (30.82, 32.65)	31.57 (30.38, 32.77)	32.35 (30.03, 34.68)	0.285	0.153
Multivariate adjusted	35.23 (33.59, 36.88)*	33.00 (31.94, 34.06)	31.76 (30.90, 32.63)	30.46 (29.29, 31.62)	30.57 (28.30, 32.83)	**<0.001**	0.110
Systolic BP (mmHg)							
Age- and sex-adjusted	130.40 (125.43, 135.38)	129.44 (126.11, 132.76)	129.93 (127.13, 132.73)	130.11 (126.47, 133.75)	131.12 (124.03, 138.21)	0.825	0.701
Multivariate adjusted	132.45 (127.03, 137.87)	130.28 (126.77, 133.78)	129.60 (126.74, 132.46)	129.02 (125.17, 132.86)	129.48 (122.04, 136.92)	0.513	0.572
Multivariate + BMI	132.48 (126.94, 138.02)	130.29 (126.76, 133.81)	129.60 (126.73, 132.46)	129.00 (125.12, 132.89)	129.47 (121.99, 136.94)	0.515	0.571
Diastolic BP (mmHg)							
Age and sex adjusted	77.82 (75.15, 80.49)	74.75 (72.97, 76.53)	76.54 (75.04, 78.04)	76.20 (74.25, 78.15)	76.69 (72.89, 80.50)	0.875	0.325
Multivariate adjusted	78.78 (75.87, 81.70)	75.28 (73.39, 77.17)	76.18 (74.64, 77.72)	75.79 (73.72, 77.85)	76.18 (72.17, 80.18)	0.427	0.205
Multivariate + BMI	78.44 (75.47, 81.41)	75.20 (73.31, 77.09)	76.22 (74.68, 77.76)	75.96 (73.87, 78.04)	76.34 (72.32, 80.35)	0.567	0.245
HbA_{1c} (%)							
Age- and sex-adjusted	6.63 (6.36, 6.90)	6.80 (6.62, 6.97)	6.53 (6.38, 6.68)	6.63 (6.44, 6.83)	6.79 (6.41, 7.17)	0.750	0.484
Multivariate adjusted	6.63 (6.36, 6.90)	6.74 (6.57, 6.92)	6.56 (6.42, 6.71)	6.64 (6.44, 6.83)	6.79 (6.42, 7.17)	0.688	0.482
Multivariate + BMI	6.60 (6.32, 6.88)	6.74 (6.56, 6.91)	6.57 (6.43, 6.71)	6.65 (6.46, 6.85)	6.81 (6.43, 7.18)	0.551	0.546
Triacylglycerol (mmol/l)[a]							
Age- and sex-adjusted	1.75 (1.49, 2.05)	1.63 (1.46, 1.80)	1.55 (1.42, 1.70)	1.67 (1.48, 1.86)	2.12 (1.70, 2.66)*	0.175	**0.014**
Multivariate adjusted	1.66 (1.40, 1.97)	1.58 (1.41, 1.76)	1.58 (1.45, 1.73)	1.73 (1.53, 1.95)	2.16 (1.71, 2.75)*	0.075	**0.035**
Multivariate + BMI	1.59 (1.33, 1.89)	1.56 (1.40, 1.74)	1.59 (1.46, 1.74)	1.76 (1.56, 1.99)	2.21 (1.75, 2.80)*	**0.026**	**0.059**
Total cholesterol (mmol/l)							
Age- and sex-adjusted	4.40 (4.14, 4.66)	4.22 (4.05, 4.39)	4.25 (4.11, 4.40)	4.39 (4.20, 4.57)	4.34 (3.97, 4.71)	0.919	0.440
Multivariate adjusted	4.30 (4.04, 4.56)	4.21 (4.04, 4.38)	4.29 (4.15, 4.42)	4.41 (4.22, 4.59)	4.30 (3.95, 4.66)	0.696	0.958
Multivariate + BMI	4.29 (4.03, 4.56)	4.21 (4.04, 4.37)	4.29 (4.15, 4.42)	4.41 (4.22, 4.60)	4.31 (3.95, 4.67)	0.664	0.977
HDL-cholesterol (mmol/l)							
Age- and sex-adjusted	1.23 (1.15, 1.32)	1.18 (1.12, 1.23)	1.21 (1.16, 1.25)	1.21 (1.15, 1.27)	0.99 (0.87, 1.10)*	**0.004**	**0.023**
Multivariate adjusted	1.23 (1.14, 1.32)	1.19 (1.13, 1.25)	1.21 (1.16, 1.25)	1.20 (1.13, 1.26)	0.98 (0.86, 1.11)*	**0.009**	**0.018**
Multivariate + BMI	1.25 (1.16, 1.34)	1.20 (1.14, 1.26)	1.20 (1.15, 1.25)	1.18 (1.12, 1.25)	0.97 (0.85, 1.09)*	**0.002**	**0.031**
LDL-cholesterol (mmol/l)							
Age- and sex-adjusted	2.26 (2.02, 2.49)	2.28 (2.12, 2.43)	2.28 (2.15, 2.41)	2.38 (2.22, 2.55)	2.38 (2.05, 2.70)	0.424	0.902
Multivariate adjusted	2.20 (1.97, 2.42)	2.27 (2.13, 2.42)	2.31 (2.20, 2.43)	2.37 (2.22, 2.53)	2.33 (2.03, 2.63)	0.415	0.580
Multivariate + BMI	2.21 (1.98, 2.43)	2.28 (2.13, 2.42)	2.31 (2.19, 2.43)	2.37 (2.21, 2.53)	2.33 (2.03, 2.63)	0.463	0.604

Numbers in parentheses represent the 95% Confidence Intervals.
Age- and sex-adjusted models also included adjustment for trial arm. Multivariate-adjusted models included age, sex, trial arm, occupational socio-economic class, PAEE, sedentary time, smoking status, alcohol consumption, self-reported feelings of tiredness, mental health score, and sleep affecting medication.
Systolic and diastolic blood pressure were additionally adjusted for prescription of anti-hypertensive drugs; HbA_{1c} was additionally adjusted for prescription of glucose lowering drugs; triacylglycerol, total cholesterol, HDL- and LDL-cholesterol were additionally adjusted for prescription of lipid-lowering drugs.
[a] Data are geometric means (95% CIs).
* Denotes significant difference from those sleeping 7 to <8 h/night at $p < 0.05$ using Dunnett's significant difference comparison.

duration was inversely associated with waist circumference and BMI (p linear trend both <0.001), such that participants sleeping 7 to <8 h/night had a 7.9 cm lower waist circumference and 3.5 kg/m^2 lower BMI than those sleeping <6 h/night ($p < 0.05$). In adjusted analyses, triacylglycerol levels were lowest among participants sleeping 7 to <8 h/night, and were significantly lower when compared with those sleeping ≥9 h/night ($p < 0.05$). HDL-cholesterol levels did not differ across sleep categories except for individuals sleeping ≥9 h/night, among whom levels were significantly lower than those sleeping 7 to <8 h/night (mean 0.98 mmol/l (95% CI: 0.86, 1.11) vs. 1.21 mmol/l (95% CI: 1.16, 1.25), respectively). We found no consistent associations between sleep duration and systolic or diastolic blood pressure, HbA_{1c}, total cholesterol or LDL-cholesterol, although the lowest levels tended to be observed among those sleeping 7 to <8 h/night.

We found no evidence of interaction by sex (all p values: ≥ 0.08) except for the association with diastolic blood pressure (p for interaction: 0.03). When stratified by sex, men sleeping 6 to <7 h/night had a diastolic blood pressure 9.53 mmHg (95% CI: 5.29, 13.77) higher than women sleeping 6 to <7 h/night; no other differences between men and women across sleep categories were found. Additional adjustment for total energy intake in the multivariate models did not materially change our findings (data not shown). Using a cut-point of ≤1.00 MET to define sleep, as opposed to a cut-point of ≤1.04 METs, did not materially change our findings (data not shown).

4. Discussion

This study demonstrates that patients with type 2 diabetes who sleep 7 to <8 h per night have a better cardiometabolic risk profile, including measures of waist circumference, BMI, triacylglycerol and HDL-cholesterol than those who sleep <6 h or >9 h per night. To the best of our knowledge, this is the first epidemiological study that investigates the association between objectively measured sleep duration and a wide range of cardiovascular risk factors independent of potential confounding by objectively measured physical activity and sedentary time. Our findings support the hypothesis that sleep duration is a potentially important and modifiable behaviour related to cardiometabolic risk in individuals with type 2 diabetes who are at high risk of cardiovascular disease.

An inverse association between sleep duration and anthropometric measures is consistent with previous literature. In a meta-analysis of 18 cross-sectional studies, which included a total of >604,000 adults [35], each additional hour of sleep was found to be associated with a pooled β-coefficient for BMI of –0.35 kg/m^2 (95% CI: –0.57, –0.12). Several [6,7], but not all [36], prospective studies have also reported inverse associations between sleep duration and weight gain. For example, in the Quebec Family Study cohort, individuals sleeping 5–6 h/day gained 1.98 (95% CI: 1.16, 2.82) kg more than those sleeping an average of 7–8 h/day, over a period of 6 years [6]. Additionally, the risk for developing obesity was shown to be 27% higher among short duration sleepers compared with those sleeping 7–8 h/day after six years of follow-up. Several studies have indicated that a J-shaped association may exist between sleep duration and weight in healthy adults, such that sleeping >8 h/day is similarly related to excess weight as sleeping too few hours [37]. However, we did not find strong evidence indicative of deviation from linearity, which is consistent with a recent study in individuals with type 2 diabetes [18]. Previous studies have found that sleep restriction can adversely affect glucose metabolism in response to a glucose challenge, but not fasting glucose or insulin levels [5,38]. A recent cross-sectional study also reported no association between sleep duration and fasting glucose, insulin or the homeostatic model assessment (HOMA) index in individuals with or without type 2 diabetes [20], which is consistent with our finding of no clear association between sleep duration and HbA_{1c}.

Previous studies examining the association between sleep duration and lipid levels have yielded mixed results [17,39,40]. Consistent with our findings, it has previously been shown that longer sleep durations are associated with relatively higher triacylglycerol levels and lower HDL-cholesterol levels [40]. In a cross-sectional study comprised mostly of participants free from diabetes, it was also observed that individuals sleeping >8 h per night had a borderline significantly lower HDL-cholesterol level relative to individuals sleeping 7–8 h per night [39]. However, in a similar study to ours, but which included only women with diabetes, Williams et al. [17] found no association between sleep duration and lipid levels, although HDL-cholesterol levels did appear to increase with increasing sleep duration, but only among normotensive individuals.

In the NHANES study, sleeping ≤5 h compared with sleeping 7–8 h per night was associated with a 60% higher risk of hypertension in healthy adults aged 32–59 years, but not among individuals aged over 60 years [8]. In a prospective analysis of sleep duration and hypertension in the Whitehall-II study [41], a non-significant inverse association between sleep duration and hypertension was found among women, but not men, sleeping ≤5 h per night. In our study, we observed no clear associations between sleep duration and blood pressure across sleep duration categories. Explanations for differences between study findings, other than diabetes status, might be the method used for sleep assessment, differences in the age of the participants and differences in covariate selection and adjustment.

The biological mechanisms underlying the relationship between short sleep duration and cardiometabolic risk factors remain to be fully elucidated, but several plausible mechanisms have been suggested in relation to the risk of overweight and obesity [12]. One plausible mechanism to explain our finding is provided by Spiegel et al. [4]. In a randomised crossover trial which involved two days of sleep restriction preceded/followed by two days of sleep extension, Spiegel et al. showed that the appetite-stimulating hormone, ghrelin, increased by 28% whereas the appetite suppressing hormone, leptin, decreased by 18% following the two days of sleep restriction. As a result, appetite increased by 23%, especially for calorie-dense, high-carbohydrate foods. To examine whether the association between sleep duration and anthropometric measures was mediated by energy intake in our analyses, we additionally adjusted for total energy intake, but this did not materially change our findings, suggesting that our findings are unlikely explained by self-reported increased food intake. As short sleep duration can also increase feelings of fatigue [42], which may lead to relative reductions in physical activity [43] and RMR [44], this may also partly explain the associations we observed. Indeed, we did find that participants sleeping 7 to <8 h per night tended to be more physically active and less sedentary than those sleeping <7 h per night (when expressed relative to time awake).

The current study has a number of strengths. First, to derive sleep duration, we used a combination of self-report questionnaire and objectively measured free-living data from a combined heart rate and movement sensor worn continually for four days, unlike previous studies which have tended to use self-report data only [13]. While this method has not been used previously, our MET definition of sleep has been shown to be consistent with a posture indicative of sleep as opposed to a seated posture [30]. MET thresholds are commonly used in the scientific literature to define both low-energy-expenditure activities such as reading and watching television as well as vigorous intensity activities such as running [45]. In addition, combining self-report and objective data for the assessment of sleep duration has been recommended in order to overcome the limitations of subjective and objective data when used in isolation [46]. Unlike previous studies, a major strength of our

study was that we accounted for objectively measured physical activity and sedentary time in our models, both of which differ by sleep duration. Our study also has a number of limitations. The cross-sectional analysis of our study precludes inference of the direction or causal nature of the observed associations. As such, it is equally plausible that obesity may have influenced sleep duration. However, our results are consistent with the epidemiological evidence indicating that short sleep duration is adversely associated with cardiovascular risk factors [6–9,13,33,47]. We were unable to account for potential confounding by sleep apnoea, the prevalence of which may be as high as 83% in patients with type 2 diabetes [48]. Nevertheless, we have adjusted our analyses for several factors known to be associated with sleep apnoea, and which are currently used for the screening of sleep apnoea (ie, Berlin Questionnaire [49]), including age, sex, feelings of daytime tiredness and BMI. Finally, although we included many potential confounding variables we cannot exclude the possibility of residual confounding, for example, by variation in daytime napping. To address the limitations of the current study, future well-designed prospective studies are needed which have measures of sleep duration, physical activity, and sedentary time and which also account for potential confounding by sleep apnoea and sleep quality.

In summary, our results provide further evidence of the potentially important role of sleep on cardiometabolic risk in people with type 2 diabetes. Examining the prospective association between sleep duration and a wide range of cardiometabolic risk factors, and the likely multiple determinants of sleep duration, will be important for improving the future design of lifestyle interventions aimed at reducing cardiovascular morbidity in this high-risk population.

Author contributions

AJMC had full access to all the data in the study and takes responsibility for the accuracy of the data analysis. SJG is a principal investigator for the ADDITION-Plus trial. AJMC, SJG and RKS are the guarantors of this work and, as such, had full access to all data in the study and take responsibility for the integrity of the data. SJG acquired the data. AJMC, SJG and RKS conceived and designed the study. AJMC and KW analysed the data and AJMC, KW, SB, ATP, SJG and RKS interpreted the data. AJMC drafted the manuscript, and all authors critically revised the manuscript for important intellectual content and have approved the final version.

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Conflict of interest

The authors declare that they have no competing interests.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.10.006.

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